Lo studio FIGARO

Paola Fioretto
Dipartimento di Medicina
Università di Padova

800 ANNI 1222-2022 UNIVERSITÀ DEGLI STUDI DI PADOVA

FIGARO-DKD rationale

FIDELIO-DKD[1]
FInerenone in reducing kiDnEy faiLure and dIsease prOgression in DKD

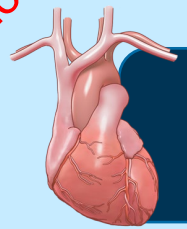
- **FIDELIO-DKD** assessed the effects of finerenone on slowing CKD progression and reducing CV mortality and morbidity in patients with CKD and T2D
- Most patients included in the FIDELIO-DKD trial had **advanced CKD** (stages 3–4)

Complementary study

FIGARO-DKD[2]
FInerenone in reducinG cArdiovascular moRtality and mOrbidity in DKD

FIGARO-DKD was designed to test whether finerenone reduced **CV mortality and morbidity** in **patients with earlier stages of CKD, including:**

- Patients with **stage 2–4 CKD and moderately elevated albuminuria**, or
- Patients with **stage 1–2 CKD with severely increased albuminuria**



A patient population at **high CV risk** that was **excluded from or understudied in FIDELIO-DKD**

1. Bakris GL, *et al*. *N Engl J Med* 2020;383:2219–2229; 2. Ruilope LM, *et al*. *Am J Nephrol* 2019;50:345–356

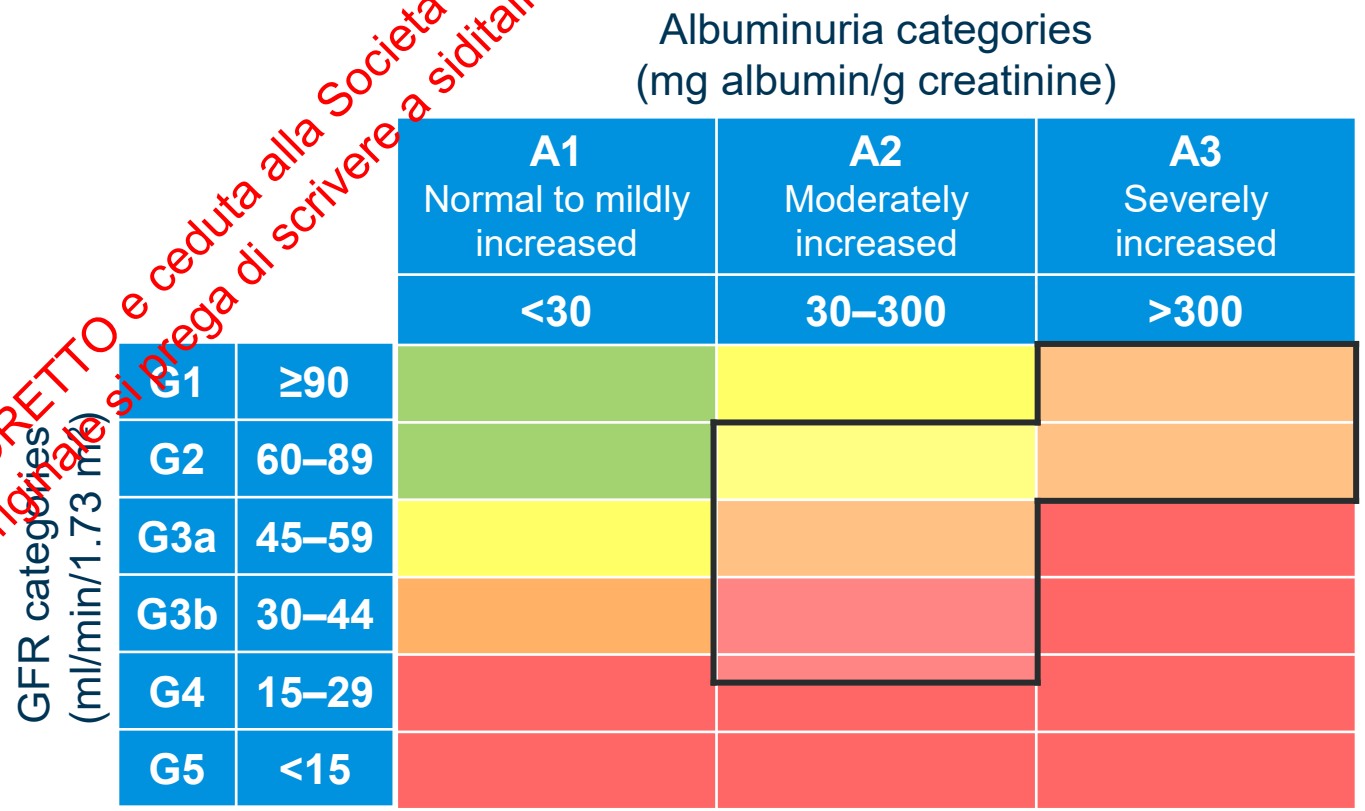
FIGARO-DKD included a broad patient population across early-to-late disease stages of CKD in T2D

Inclusion criteria

- T2D and CKD, defined as **either:**
  - UACR 30–300 mg/g and eGFR ≥25–≤90 ml/min/1.73 m^2 **or**
  - UACR ≥300–≤5000 mg/g and eGFR ≥60 ml/min/1.73 m^2
- Treated with either an ACEi or an ARB at maximum tolerated dose
- Serum [K^+] ≤4.8 mmol/l

Key exclusion criteria

- Non-diabetic kidney disease
- Uncontrolled hypertension*
- HbA1c >12%
- **Chronic symptomatic HFrEF#**
- Recent CV event
- Dialysis for acute kidney failure
- Kidney transplant



FIGARO-DKD was a randomised, double-blind, event-driven, placebo-controlled phase III trial

19,381 patients enrolled

Run-in
4–16 weeks
Optimisation of ACEi or ARB therapy

Screening
≤2 weeks

R*

7437 patients randomised

Finerenone (initial dose 10 or 20 mg od#)
Post-treatment follow-up

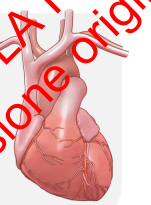
Placebo (initial dose 10 or 20 mg od#)
Post-treatment follow-up

3.4 years' median follow-up

Key endpoints

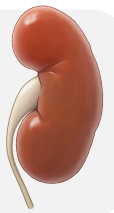
1. CV composite

Time to CV death,‡ non-fatal MI, non-fatal stroke or hospitalisation for HF



2. Kidney composite

Time to kidney failure,§ sustained ≥40% decrease in eGFR from baseline,¶ or renal death**



At baseline, patients had well-controlled blood pressure and HbA1c

Selected baseline characteristic	Finerenone (n=3686)	Placebo (n=3666)
Age, years, mean ± SD	64.1±9.2	64.1±10.0
Male, n (%)	2528 (68.6)	2577 (70.3)
BMI, kg/m^2, mean ± SD	31.5±6.0	31.4±5.9
Duration of T2D, years, mean ± SD	14.5±8.6	14.4±8.4
Systolic blood pressure, mmHg, mean ± SD	135.8±14.0	135.7±14.1
Diastolic blood pressure, mmHg, mean ± SD	76.8±9.5	76.8±9.6
HbA1c, %, mean ± SD	7.7±1.4	7.7±1.4
Glucose-lowering therapies, n (%)	3607 (97.9)	3589 (97.9)
Insulin	2023 (54.9)	1970 (53.7)
Metformin	2561 (69.5)	2506 (68.4)
SGLT-2i	314 (8.5)	304 (8.3)
GLP-1RA	308 (8.4)	242 (6.6)

Bakris GL, *et al*. *N Engl J Med* 2020;383:2219–2229

At baseline, patients had mild to moderate CKD, and most had UACR ≥30 mg/g and were treated with the maximum tolerated dose of an ACEi or ARB

Selected baseline characteristic		Finerenone (n=3686)	Placebo (n=3666)
eGFR,* ml/min/1.73 m^2, mean ± SD		67.6±21.7	68.0±21.7
eGFR* at baseline, ml/min/1.73 m^2, n (%)	<25	15 (0.4)	12 (0.3)
	25–<45	641 (17.4)	610 (16.6)
	45–<60	745 (20.2)	789 (21.5)
	≥60	2285 (62.0)	2254 (61.5)
Median UACR, mg/g (IQR)		302 (105–749)	315 (111–731)
UACR at baseline, mg/g, n (%)*	≥300	1851 (50.2)	1878 (51.2)
	30–<300	1726 (46.8)	1688 (46.0)
	<30	109 (3.0)	98 (2.7)
Serum [K^+], mmol/l, mean ± SD		4.33±0.43	4.33±0.43
ACEi, n (%)		1576 (42.8)	1561 (42.6)
ARB, n (%)		2108 (57.2)	2104 (57.4)

Bakris GL, *et al. N Engl J Med* 2020;383:2219–2229

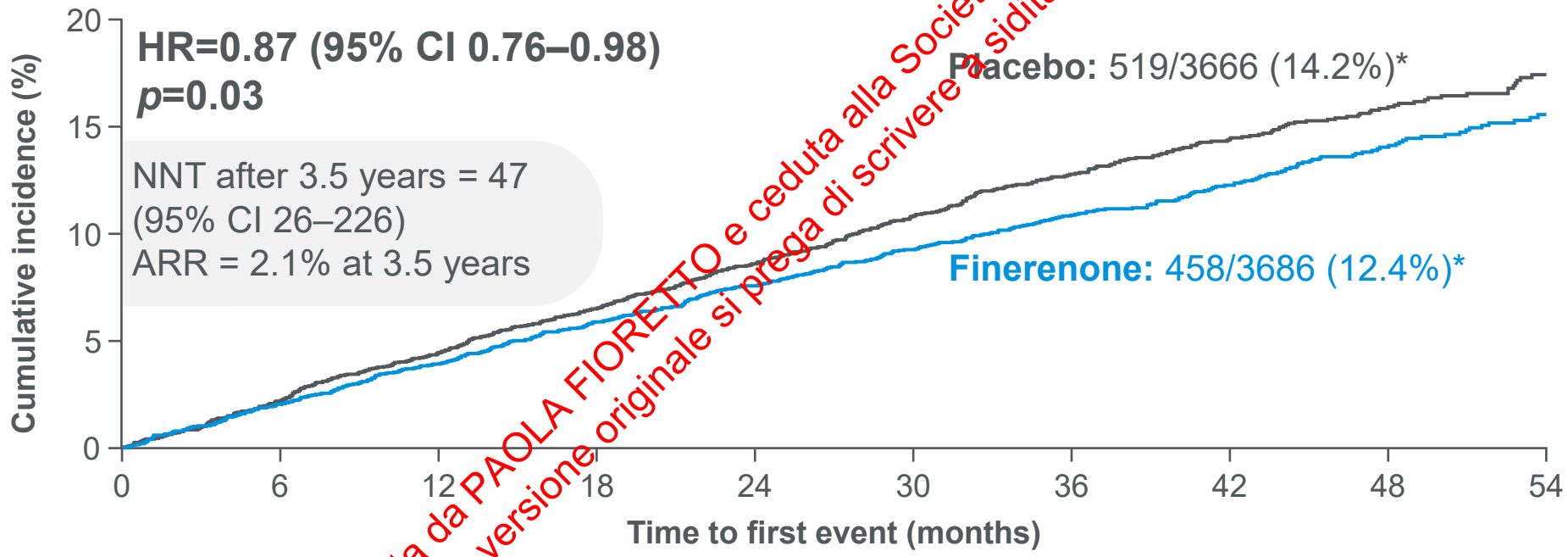
At baseline, almost half of the patients had a history of CV disease, with coronary artery disease being the most common

Medical history at baseline, n (%)	Finerenone (n=3666)	Placebo (n=3666)
Diabetic retinopathy	1193 (32.4)	1098 (30.0)
Hypertension	3544 (96.1)	3517 (95.9)
History of CV disease	1676 (45.5)	1654 (45.1)
Coronary artery disease	1148 (31.1)	1147 (31.3)
Myocardial infarction	640 (17.4)	616 (16.8)
Peripheral artery disease	587 (15.9)	575 (15.7)
Ischaemic stroke	442 (12.0)	425 (11.6)
Heart failure	290 (7.9)	281 (7.7)
Diabetic neuropathy	1046 (28.4)	990 (27.0)

Bakris GL, *et al*. *N Engl J Med* 2020;383:2219–2229

On top of maximum tolerated RAS therapy, finerenone significantly reduced the risk of the primary CV outcome by 13%

Time to CV death, non-fatal MI, non-fatal stroke or HHF



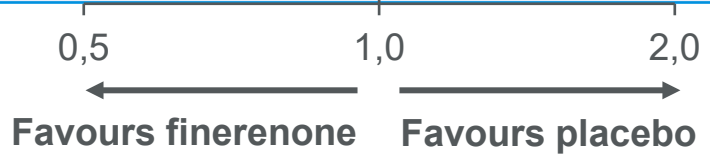
No. at risk

Finerenone	3686	3600	3517	3427	3320	2781	2184	1712	1093	598
Placebo	3666	3577	3479	3389	3267	2730	2125	1657	1076	585

- Bakris GL, *et al*. *N Engl J Med* 2020;383:2219–2229

Finerenone had consistent effects on CV death, stroke, MI and hospitalisation for HF

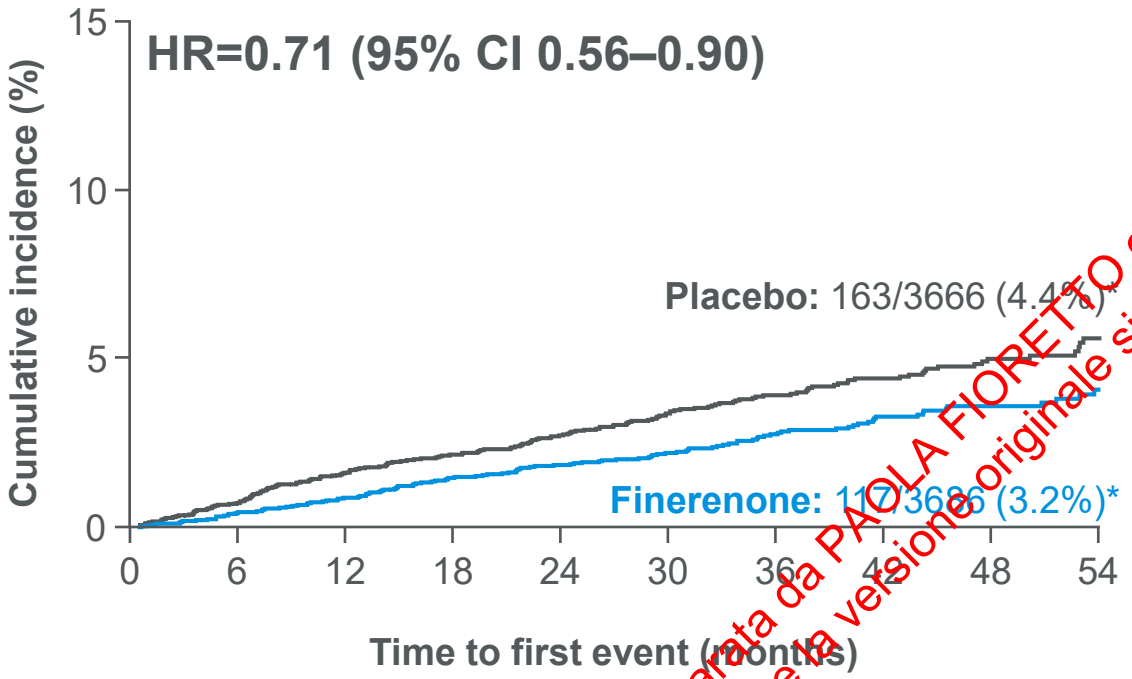
Outcome	Finerenone (n=3686)		Placebo (n=3666)		HR (95% CI)	*p*-value
	n (%)	n/100 PY	n (%)	n/100 PY		
Primary composite CV outcome*	**458 (12.4)**	**3.87**	**519 (14.2)**	**4.45**	**0.87 (0.76–0.98)**	**0.03**
CV death	194 (5.3)	1.56	214 (5.8)	1.74	0.90 (0.74–1.09)	–
Non-fatal MI	103 (2.8)	0.85	102 (2.8)	0.85	0.99 (0.76–1.31)	–
Non-fatal stroke	108 (2.9)	0.89	111 (3.0)	0.92	0.97 (0.74–1.26)	–
Hospitalisation for HF	117 (3.2)	0.96	163 (4.4)	1.36	0.71 (0.56–0.90)	–



Bakris GL, *et al*. *N Engl J Med* 2020;383:2219–2229

Primary outcome components: Risk of HHF reduced by 29% and incidence of CV death was numerically lower with finerenone vs placebo

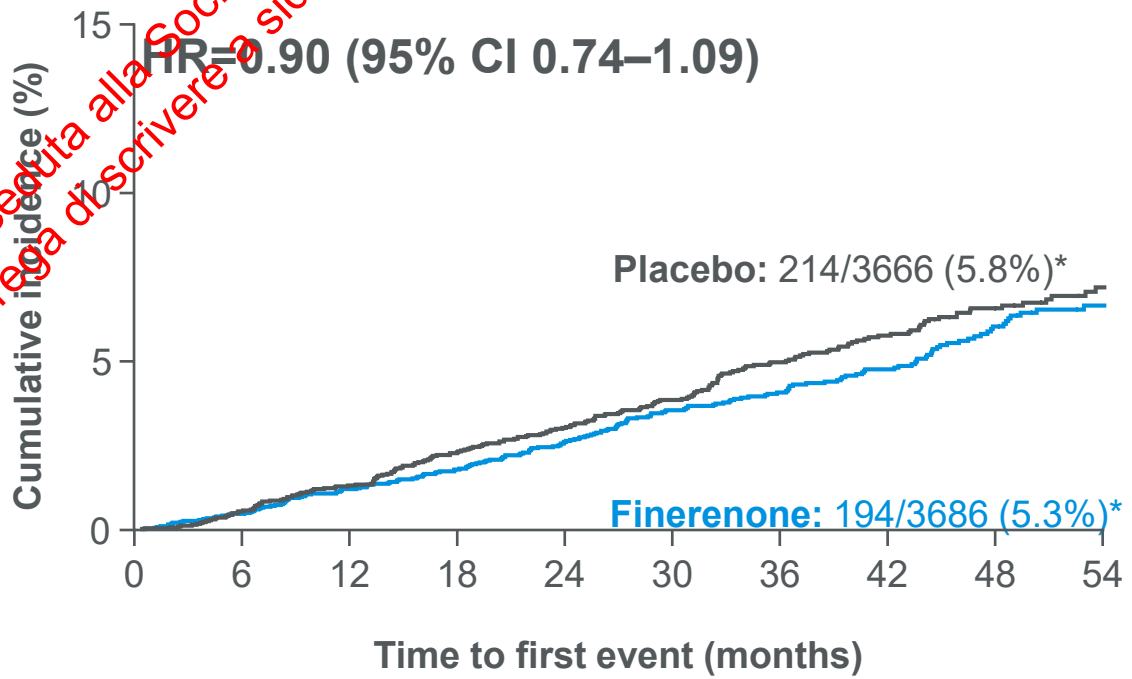
HHF (time to first event)



No. at risk

3686	3640	3581	3515	3429	2881	2284	1790	1142	629
3666	3610	3538	3471	3376	2840	2239	1751	1134	619

CV death (time to first event)



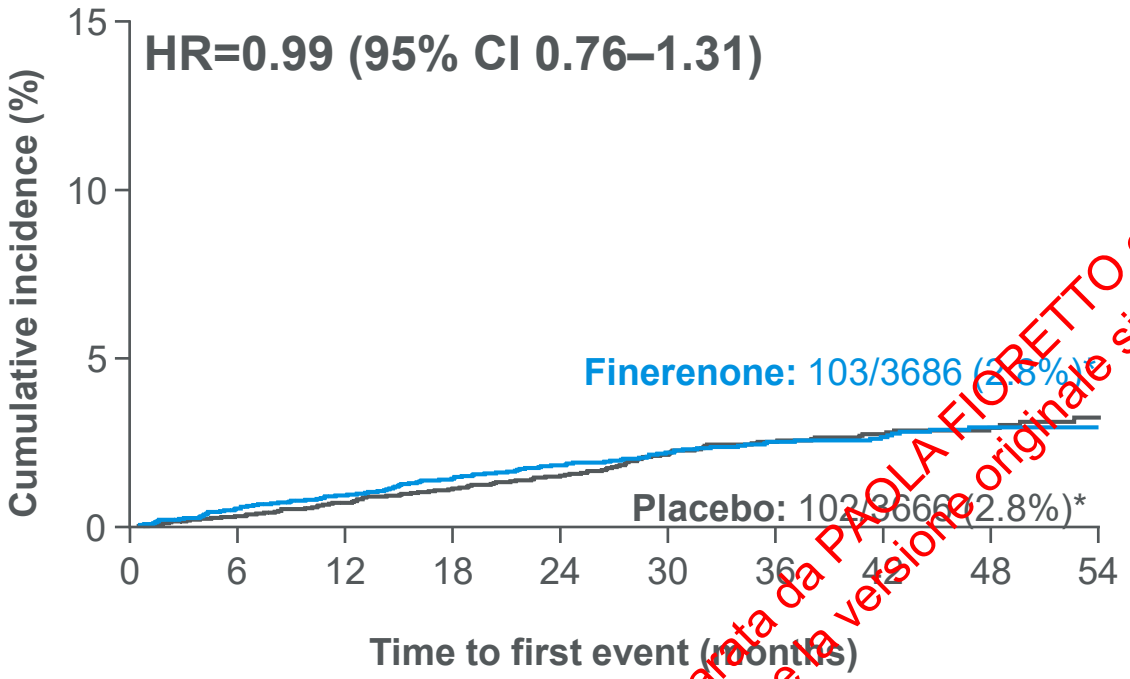
No. at risk

3686	3661	3620	3581	3503	2968	2358	1858	1187	653
3666	3639	3593	3539	3468	2938	2315	1820	1177	647

Bakris GL, *et al*. *N Engl J Med* 2020;383:2219–2229

Primary outcome components: Incidence of non-fatal stroke and non-fatal MI was similar with finerenone vs placebo

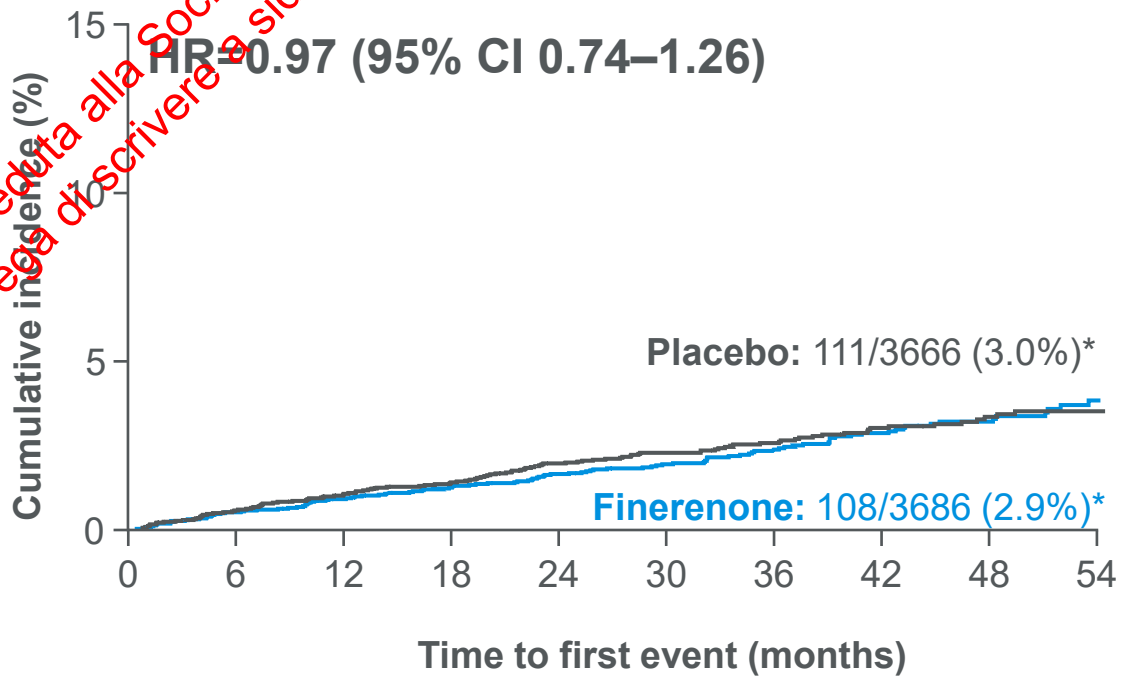
Non-fatal MI (time to first event)



No. at risk

3686	3635	3579	3522	3432	2894	2293	1809	1155	632
3666	3623	3559	3491	3404	2858	2240	1757	1135	620

Non-fatal stroke (time to first event)



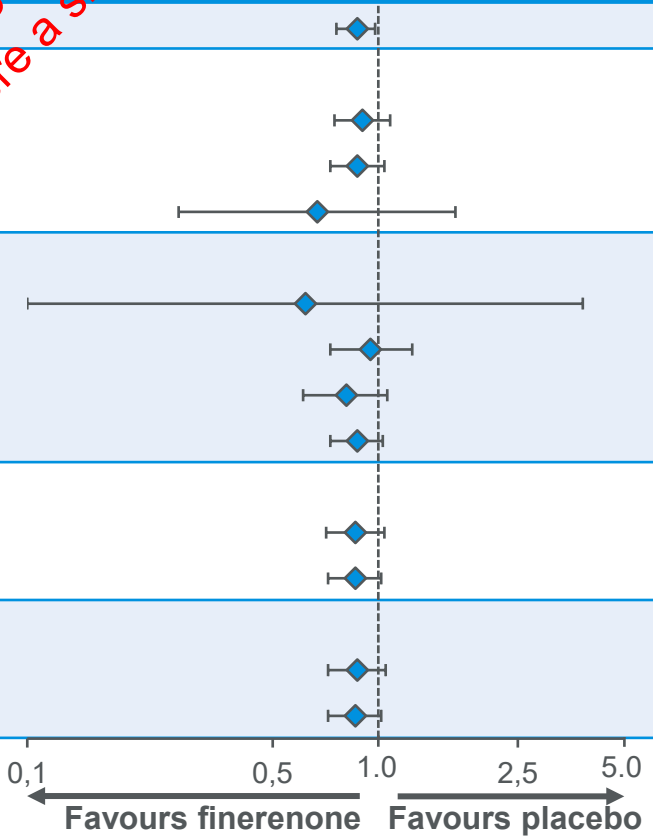
No. at risk

3686	3635	3581	3523	3433	2896	2285	1795	1145	620
3666	3614	3548	3482	3388	2860	2240	1753	1134	620

Bakris GL, *et al*. *N Engl J Med* 2020;383:2219–2229

The effects of finerenone on the primary outcome were consistent regardless of baseline UACR, eGFR, blood pressure or HbA1c

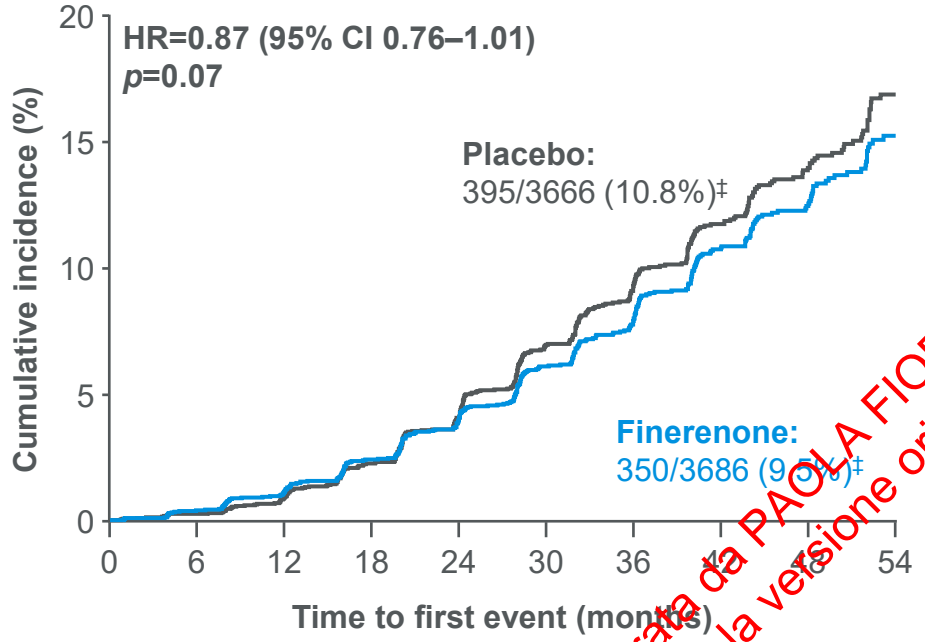
Subgroup	Finerenone (n=3686)		Placebo (n=3666)		HR (95% CI)
	n/N	n/100 PY	n/N	n/100 PY	
All patients	458/3686	3.87	519/3666	4.45	0.87 (0.76–0.98)
Baseline UACR, mg/g					
≥300	222/1851	3.94	254/1878	4.49	0.90 (0.75–1.08)
30–<300	226/1726	3.88	251/1688	4.42	0.87 (0.73–1.04)
<30	10/109	2.64	13/98	4.13	0.67 (0.27–1.66)
Baseline eGFR					
<25 ml/min/1.73 m^2	3/15	6.11	4/12	12.66	0.62 (0.10–3.83)
25–<45 ml/min/1.73 m^2	109/641	5.44	107/610	5.54	0.95 (0.73–1.25)
45–<60 ml/min/1.73 m^2	91/745	3.79	121/789	4.80	0.81 (0.61–1.06)
≥60 ml/min/1.73 m^2	255/2285	3.46	286/2254	3.99	0.87 (0.73–1.03)
Baseline SBP					
≤136.0 mmHg (median)	211/1882	3.47	234/1857	3.94	0.86 (0.71–1.04)
>136.0 mmHg (median)	247/1804	4.29	285/1809	4.54	0.86 (0.72–1.02)
Baseline HbA1c					
≤7.5%	202/1864	3.33	244/1914	3.93	0.87 (0.72–1.05)
>7.5%	253/1827	4.40	273/1746	5.03	0.86 (0.72–1.02)



Bakris GL, *et al*. *N Engl J Med* 2020;383:2219–2229

Finerenone numerically reduced the risk of both the secondary and exploratory additional composite kidney outcomes

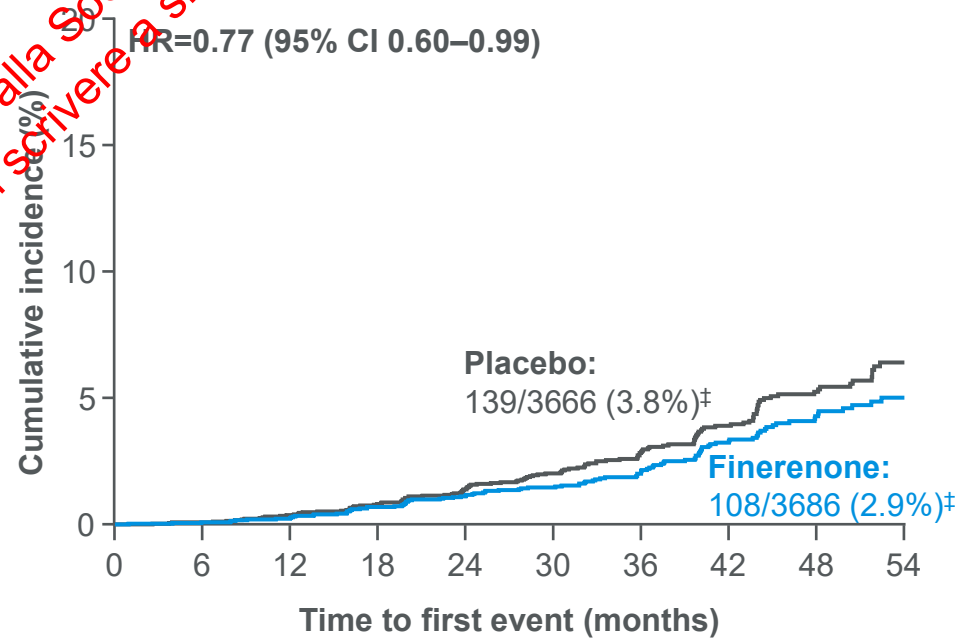
Secondary kidney composite outcome: Time to kidney failure*, sustained ≥40% decrease in eGFR from baseline, or renal death#



No. at risk

Finerenone	3686	3550	3445	3301	3131	2540	1941	1481	908	480
Placebo	3666	3546	3436	3282	3096	2507	1933	1443	907	485

Exploratory, additional kidney outcome: Time to kidney failure*, sustained ≥57% decrease in eGFR from baseline, or renal death



No. at risk

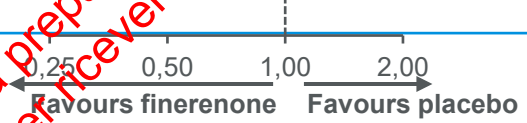
	3686	3559	3474	3356	3218	2651	2047	1582	973	522
	3666	3552	3452	3325	3178	2615	2039	1538	970	520

Bakris GL, *et al*. *N Engl J Med* 2020;383:2219–2229

Finerenone had consistent effects on the components of both the secondary and exploratory additional composite kidney outcomes

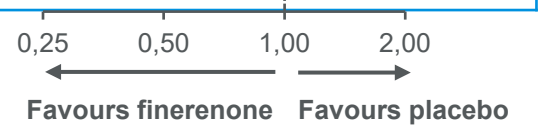
Components of the secondary kidney composite

Outcome	Finerenone (n=3686)		Placebo (n=3666)		HR (95% CI)
	n (%)	n/100 PY	n (%)	n/100 PY	
Secondary kidney outcome	350 (9.5)	3.15	395 (10.8)	3.58	0.87 (0.76–1.01)
Kidney failure*	46 (1.2)	0.40	62 (1.7)	0.54	0.72 (0.49–1.05)
ESKD	32 (0.9)	0.26	49 (1.3)	0.40	0.64 (0.41–<1.00‡)
Sustained# decrease in eGFR to <15 ml/min/1.73 m^2	28 (0.8)	0.24	38 (1.0)	0.33	0.71 (0.43–1.16)
Sustained# ≥40% decrease in eGFR	338 (9.2)	3.04	385 (10.5)	3.49	0.87 (0.75–1.00)
Renal death	0	–	2 (<0.1)	–	–



Components of the exploratory additional kidney composite

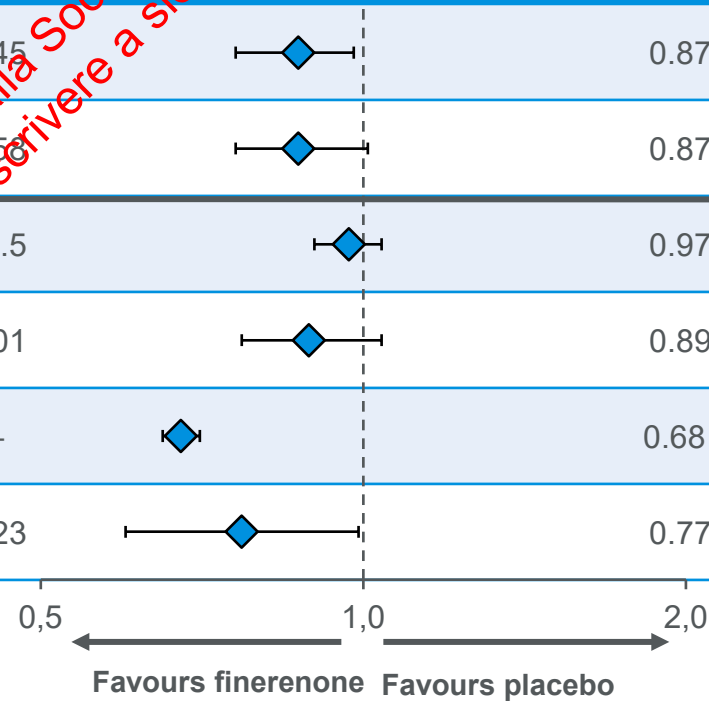
	Finerenone (n=3686)	Placebo (n=3666)	HR (95% CI)
Secondary kidney composite	108 (2.9)	139 (3.8)	0.77 (0.60–0.99)
Kidney failure*	46 (1.2)	62 (1.7)	0.72 (0.49–1.05)
Sustained# ≥57% decrease in eGFR	90 (2.4)	116 (3.2)	0.76 (0.58–1.00)
Renal death	0	2 (<0.1)	–



Bakris GL, *et al*. *N Engl J Med* 2020;383:2219–2229

The risk of the secondary kidney composite outcome was similar between groups – subsequent outcomes are exploratory

Hierarchical analysis		Outcome	Finerenone (n=3686)		Placebo (n=3666)		HR (95% CI)	*p*-value
			n (%)	n/100 PY	n (%)	n/100 PY		
1	✓	Primary composite CV outcome	458 (12.4)	3.87	519 (14.2)	4.45	0.87 (0.76–0.98)	0.03
2	✗	Secondary kidney composite outcome	350 (9.5)	3.15	395 (10.8)	3.58	0.87 (0.76–1.01)	–
3	Exploratory	Hospitalisation for any cause	1573 (42.7)	16.9	1605 (43.8)	17.5	0.97 (0.90–1.04)	–
4		Death any cause	333 (9.0)	2.68	370 (10.1)	3.01	0.89 (0.77–1.04)	–
5		Change in UACR from baseline to month 4	–	–	–	–	0.68 (0.65–0.70)*	–
6		Additional secondary composite kidney outcome	108 (2.9)	0.95	139 (3.8)	1.23	0.77 (0.60–0.99)	–



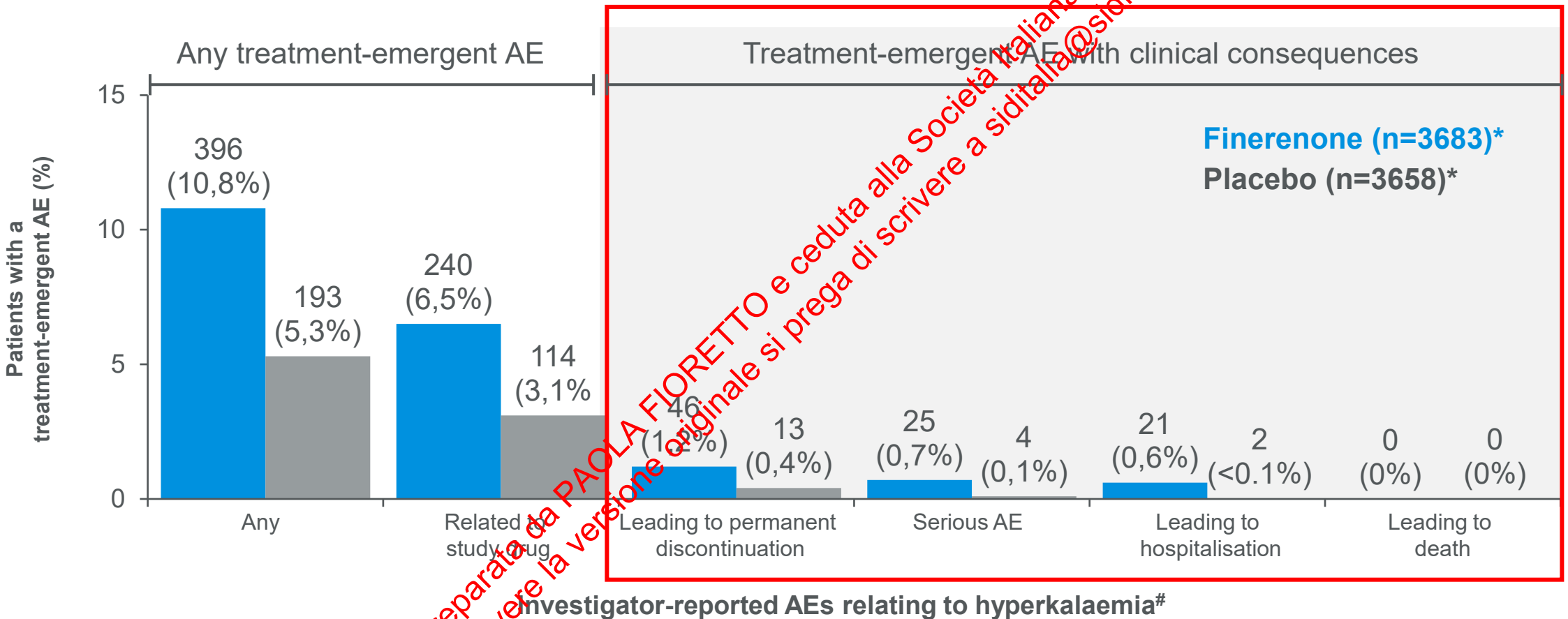
Bakris GL, *et al*. *N Engl J Med* 2020;383:2219–2229

The overall incidence of treatment-emergent adverse events was similar between the finerenone and placebo groups

Treatment-emergent adverse events, n (%)	Finerenone (n=3683)*	Placebo (n=3658)*
Any AE	3134 (85.1)	3129 (85.5)
AE related to study drug	560 (15.2)	413 (11.3)
AE leading to treatment discontinuation	207 (5.6)	183 (5.0)
Any serious AE	1158 (31.4)	1215 (33.2)
Serious AE related to study drug	35 (1.0)	27 (0.7)
Serious AE leading to treatment discontinuation	70 (1.9)	76 (2.1)
AE with outcome death	79 (2.1)	100 (2.7)

Bakris GL, *et al*. *N Engl J Med* 2020;383:2219–2229

Although investigator-reported hyperkalaemia was increased with finerenone, the clinical impact was minimal



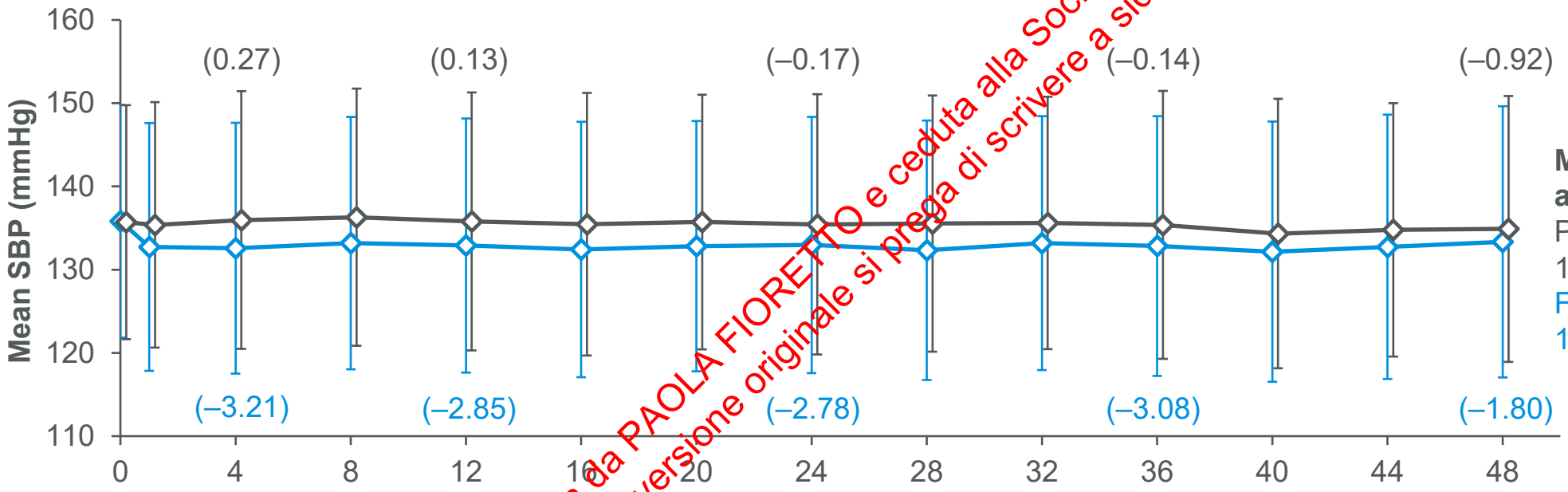
Investigator-reported AEs relating to hyperkalaemia#

There were no deaths due to hyperkalaemia, and the incidences of treatment discontinuation or hospitalisation due to hyperkalaemia were low

Bakris GL, *et al*. *N Engl J Med* 2020;383:2219–2229

Finerenone had a modest impact on blood pressure

The difference in mean SBP*# between groups was –3.5 mmHg at month 4 and –3.0 mmHg at month 12‡



Mean SBP at baseline (mmHg):
Placebo: 135.7±14.1
Finerenone: 135.8±14.0

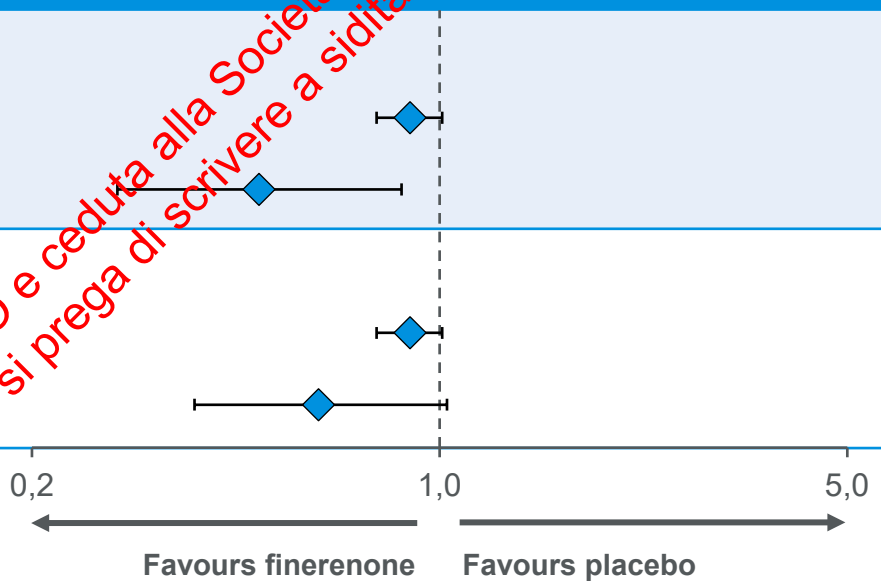
No. of patients

Finerenone	3683	3578	3442	3095	1940	854
Placebo	3658	3559	3421	3073	1930	835

- Bakris GL, *et al*. *N Engl J Med* 2020;383:2219–2229

The effects of finerenone on the primary outcome were consistent regardless of baseline use of SGLT-2is or GLP-1RAs

Category	Finerenone (n=3686)		Placebo (n=3666)		HR (95% CI)
	n/N	n/100 PY	n/N	n/100 PY	
SGLT-2i at baseline					
No	434/3372	4.01	482/3362	4.50	0.89 (0.78–1.01)
Yes	24/314	2.37	37/304	3.95	0.49 (0.28–0.86)
GLP-1RA at baseline					
No	427/3378	3.96	483/3424	4.44	0.89 (0.78–1.01)
Yes	31/308	2.97	36/242	4.69	0.62 (0.38–1.03)

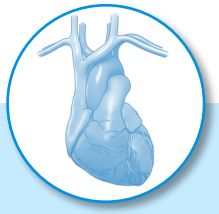


- Confidence intervals are wide in the combination therapy subgroups because of the small patient numbers and low event rates
- **Meaningful conclusions on combination therapies are not possible**

Bakris GL, *et al*. *N Engl J Med* 2020;383:2219–2229

Summary

In a patient population with mild-to-moderate CKD and T2D, well-controlled blood pressure and HbA1c, and treated with a maximum tolerated dose of an ACEi or ARB, finerenone led to:



13% (statistically significant) reduction in the risk of CV mortality and morbidity (HR=0.87; 95% CI 0.76–0.98)

13% (non-statistically significant) reduction in the risk of the ≥40% decrease in eGFR secondary kidney endpoint (HR=0.87; 95% CI 0.76–1.01)

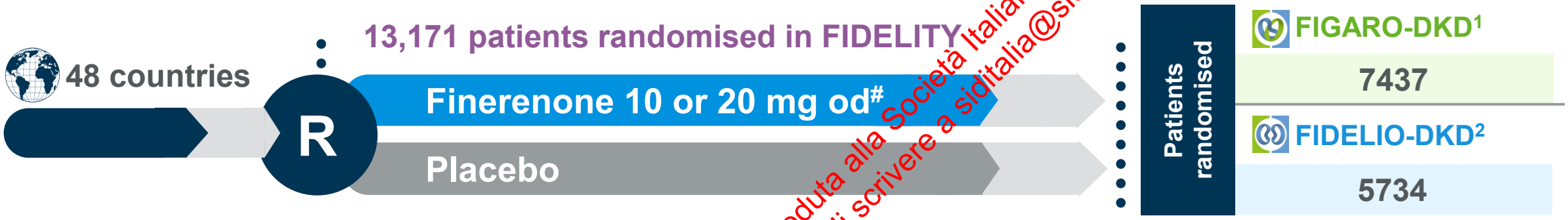
These results are supported by the effect of finerenone on the exploratory kidney-specific outcomes

Finerenone was generally well tolerated

Although the incidence of hyperkalaemia was increased, it had minimal clinical impact and was manageable by temporarily withholding treatment*

Adding to the evidence for the cardiorenal benefits of finerenone in the FIDELIO-DKD trial, the results of the FIGARO-DKD trial indicate that finerenone is an effective investigational treatment option for CV and kidney protection in patients with CKD stage 1–4 and T2D

FIGARO-DKD and FIDELIO-DKD investigated the effects of finerenone on kidney and CV outcomes in over 13,000 patients with CKD and T2D

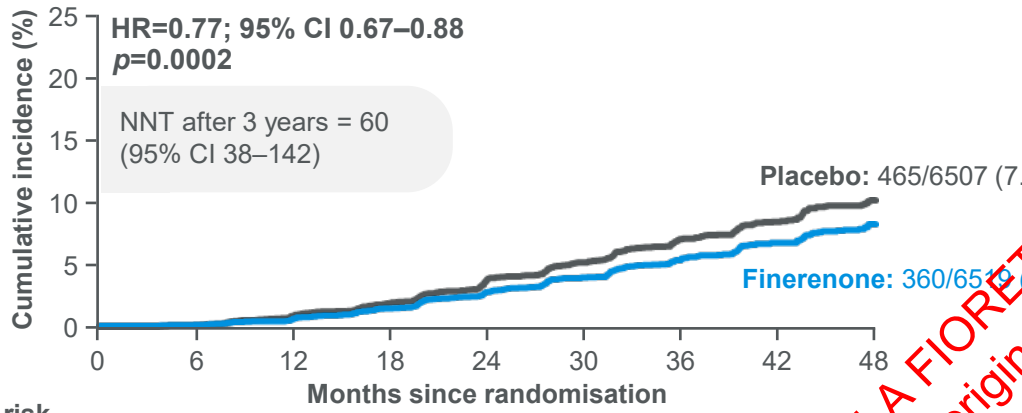


	FIGARO-DKD[1]	FIDELIO-DKD[2]	FIDELITY[3] Prespecified pooled analysis
Clinical efficacy primary endpoint	**Composite endpoint:** Time to CV death, non-fatal MI, non-fatal stroke or HHF	**Composite endpoint:** Time to kidney failure, sustained ≥40% eGFR decline or renal death	**Key outcomes** **CV composite:** Time to CV death, non-fatal MI, non-fatal stroke or HHF
Key secondary endpoint	Same as primary endpoint in **FIDELIO-DKD**	Same as primary endpoint in **FIGARO-DKD**	**57% kidney composite:** Time to kidney failure, sustained ≥57% eGFR decline or renal death

The FIDELITY primary analysis showed significant risk reductions in CV and kidney outcomes with finerenone

Kidney composite

Time to kidney failure,* sustained ≥57% decrease in eGFR from baseline, or kidney-related death

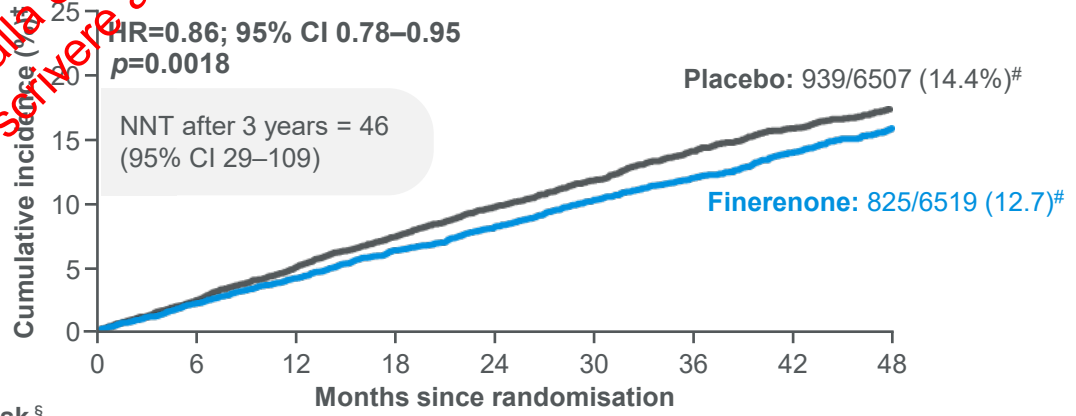


No. at risk									
Finerenone	6519	6291	6107	5848	5027	3973	2815	2024	959
Placebo	6507	6292	6071	5815	4949	3932	2798	1988	962

23% reduced **risk of CKD progression*** versus placebo (HR=0.77; 95% CI 0.67–0.88)

CV composite

Time to CV death, non-fatal MI, non-fatal stroke or HHF



No. at risk §									
Finerenone	6519	6360	6202	6009	5273	4207	3065	2187	1087
Placebo	6507	6330	6125	5938	5184	4147	2969	2135	1082

14% reduced **risk of CV morbidity and mortality** versus placebo (HR=0.86; 95% CI 0.78–0.95)

Agarwal R, et al. Eur Heart J 2022

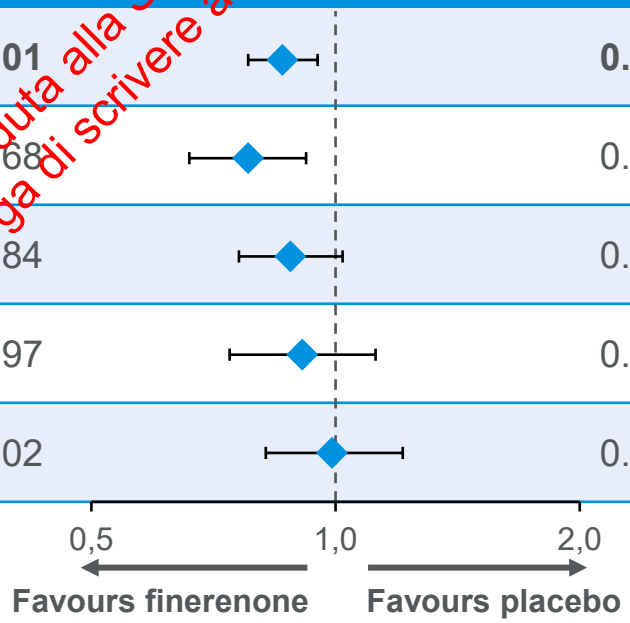
Finerenone had consistent effects on the components of the kidney composite outcome

Outcome	Finerenone (n=6519)		Placebo (n=6507)		HR (95% CI)	*p*-value
	n (%)	n per 100 PY	n (%)	n per 100 PY		
≥57% eGFR kidney composite outcome	**360 (5.5)**	**1.96**	**465 (7.1)**	**2.55**	**0.77 (0.67–0.88)**	**0.0002**
Kidney failure*	254 (3.9)	1.38	297 (4.6)	1.62	0.84 (0.71–0.99)	0.039
ESKD	151 (2.3)	0.76	188 (2.9)	0.96	0.80 (0.64–0.99)	0.040#
Sustained‡ decrease in eGFR to <15 ml/min/1.73 m^2	195 (3.0)	1.06	237 (3.6)	1.29	0.81 (0.67–0.98)	0.026#
Sustained# ≥57% decrease in eGFR from baseline	257 (3.9)	1.40	361 (5.5)	1.98	0.70 (0.60–0.83)	<0.0001
Renal death	2 (<0.1)	0.01	4 (<0.1)	0.02	0.53 (0.10–2.91)§	–

Agarwal R, et al. Eur J Heart 2022

Finerenone had consistent effects on the components of the CV composite outcome

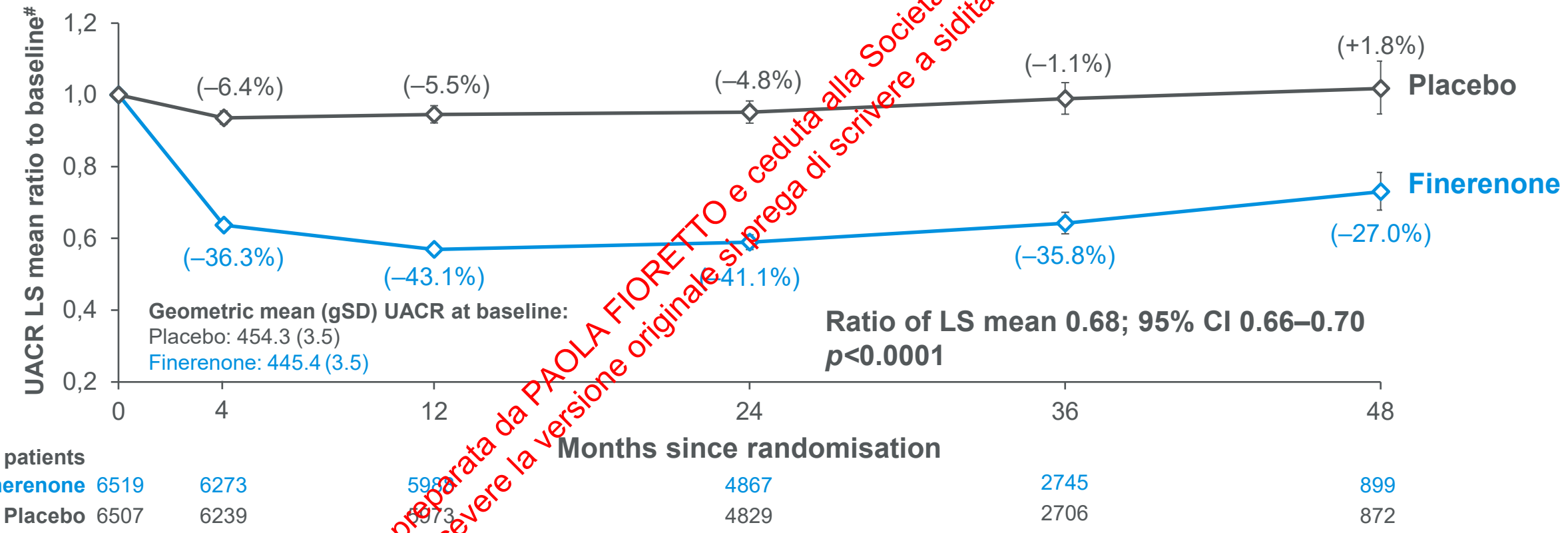
Outcome	Finerenone (n=6519)		Placebo (n=6507)		HR (95% CI)	*p*-value
	n (%)	n per 100 PY	n (%)	n per 100 PY		
Composite CV outcome	**825 (12.7)**	**4.34**	**939 (14.4)**	**5.01**	**0.86 (0.76–0.95)**	**0.0018**
Hospitalisation for HF	256 (3.9)	1.31	325 (5.0)	1.68	0.78 (0.66–0.92)	0.0030
CV death	322 (4.9)	1.61	364 (5.6)	1.84	0.88 (0.76–1.02)	0.0922
Non-fatal MI	173 (2.7)	0.88	189 (2.9)	0.97	0.91 (0.74–1.12)	0.3601
Non-fatal stroke	198 (3.0)	1.01	198 (3.0)	1.02	0.99 (0.82–1.21)	0.9460



Agarwal R, et al. Eur J Heart 2022

Effects of Finerenone on UACR

A lower mean UACR with finerenone vs placebo was maintained throughout the study



No. of patients						
Finerenone	6519	6273	5981	4867	2745	899
Placebo	6507	6239	5973	4829	2706	872

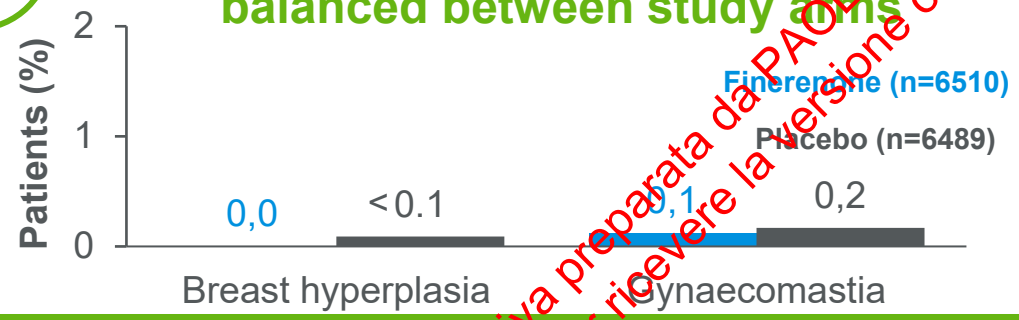
Agarwal R, et al. Eur Heart J 2022

Finerenone showed modest effects on SBP and no imbalance in sexual side effects. Overall AEs were similar between groups

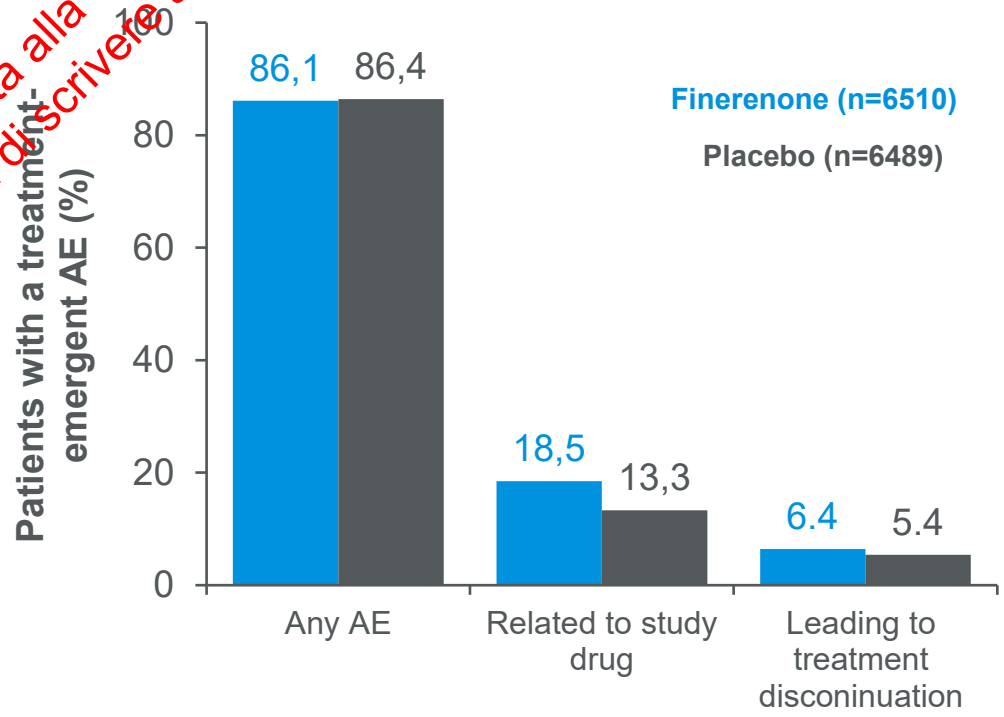
Modest effect on systolic blood pressure and no effect on HbA1c

Placebo-corrected change in mean SBP of **–3.7 mmHg** at 4 months

Sexual side effects were low and balanced between study arms



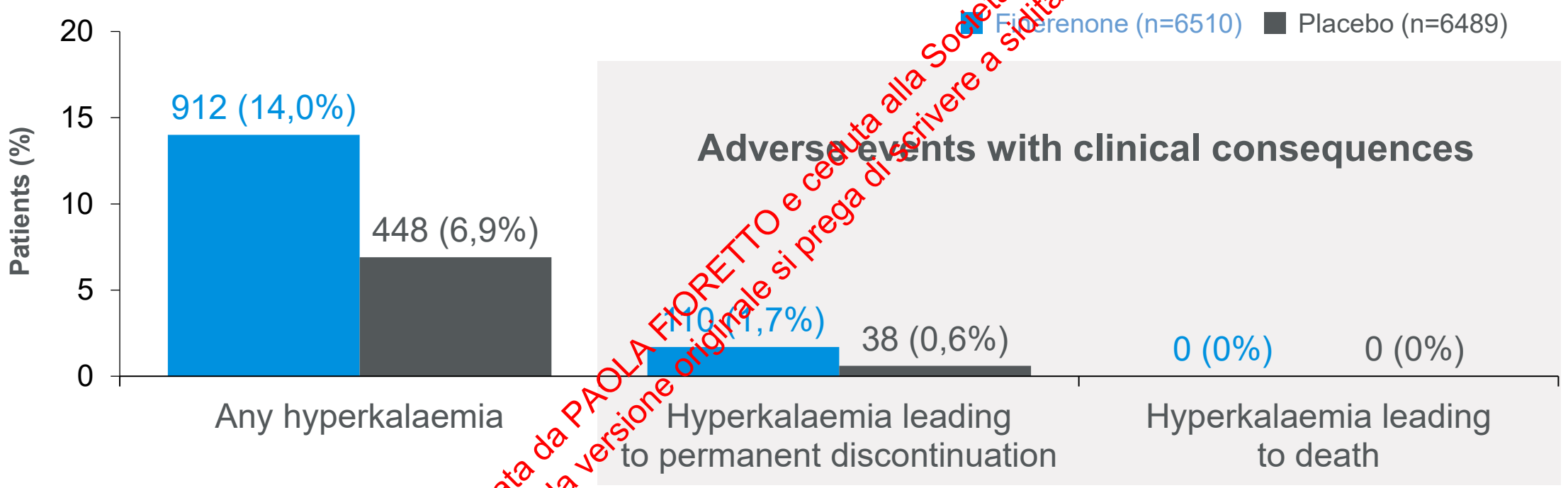
Incidence of AEs were similar between the finerenone and placebo groups



Agarwal R, et al. Eur Heart J 2022

In FIDELITY, finerenone increased hyperkalaemia

Investigator-reported hyperkalaemia adverse events*[1]



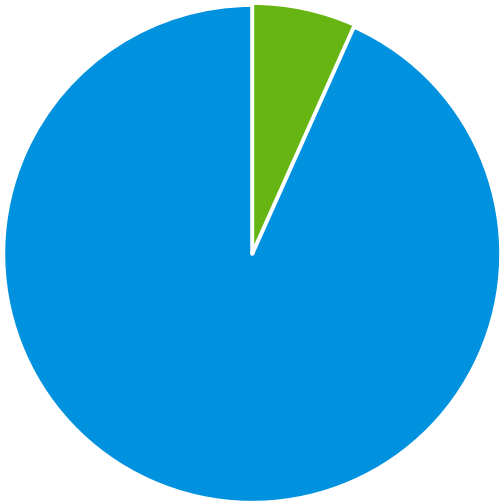
With a robust [K⁺] management strategy guided by regular serum [K⁺] monitoring, there were no hyperkalaemia-related deaths in over 13,000 patients over 3 years median follow-up[1–4]

Agarwal R, et al. JASN 2022

In FIDELITY, the effect of finerenone on UACR reduction was similar in patients treated with or without an SGLT-2i at baseline

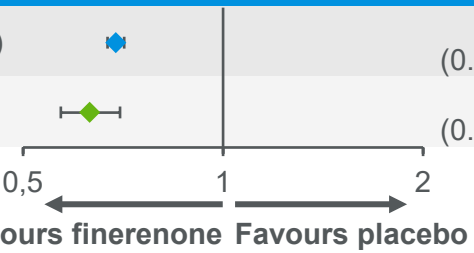
- **SGLT-2i use at baseline**

877 (6.7%) patients
on an **SGLT-2i**



- **Reduction in UACR with finerenone vs placebo at month 4**

	Finerenone, n at baseline (gMean, mg/g)	Placebo, n at baseline (gMean, mg/g)	Ratio of LS means (95% CI)	$p_{interaction}$
No SGLT-2i	6079 (449)	6065 (459)	0.69 (0.67–0.71)	0.17
SGLT-2i	438 (393)	439 (398)	0.63 (0.57–0.70)	

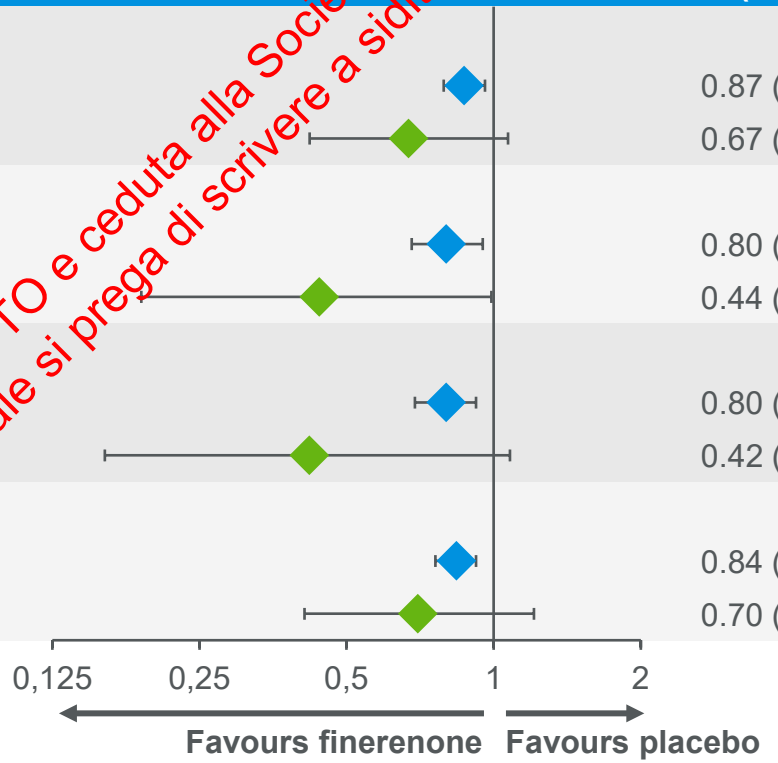


Although non-significant, the **larger UACR reduction** observed in **patients treated with finerenone in combination with SGLT-2is** (37%) vs those treated with finerenone alone (31%) suggests a **potential synergistic effect**

Rossing P, et al. Diabetes Care 2022

In FIDELITY, the CV and kidney benefits of finerenone were consistent irrespective of SGLT-2i use at baseline

Endpoint	Finerenone n/N (n/100 PY)	Placebo n/N (n/100 PY)	Adjusted HR (95% CI)*	$p_{interaction}$*
CV composite#,[1]				
No SGLT-2i	786/6081 (4.4)	887/6068 (5.1)	0.87 (0.79–0.96)	0.46
SGLT-2i	39/438 (3.0)	52/439 (4.1)	0.67 (0.42–1.07)	
HHF[1]				
No SGLT-2i	246/6081 (1.4)	303/6068 (1.7)	0.80 (0.68–0.95)	0.18
SGLT-2i	10/438 (0.7)	22/439 (1.7)	0.44 (0.19–0.99)	
eGFR 57% kidney composite‡,[1]				
No SGLT-2i	351/6081 (2.1)	448/6068 (2.6)	0.80 (0.69–0.92)	0.29
SGLT-2i	9/438 (0.7)	17/439 (1.4)	0.42 (0.16–1.08)	
eGFR 40% kidney composite§,[2]				
No SGLT-2i	818/6081 (5.0)	961/6068 (5.9)	0.84 (0.76–0.92)	0.59
SGLT-2i	36/438 (2.9)	34/439 (2.8)	0.70 (0.41–1.21)	



Rossing P, et al. Diabetes Care 2022

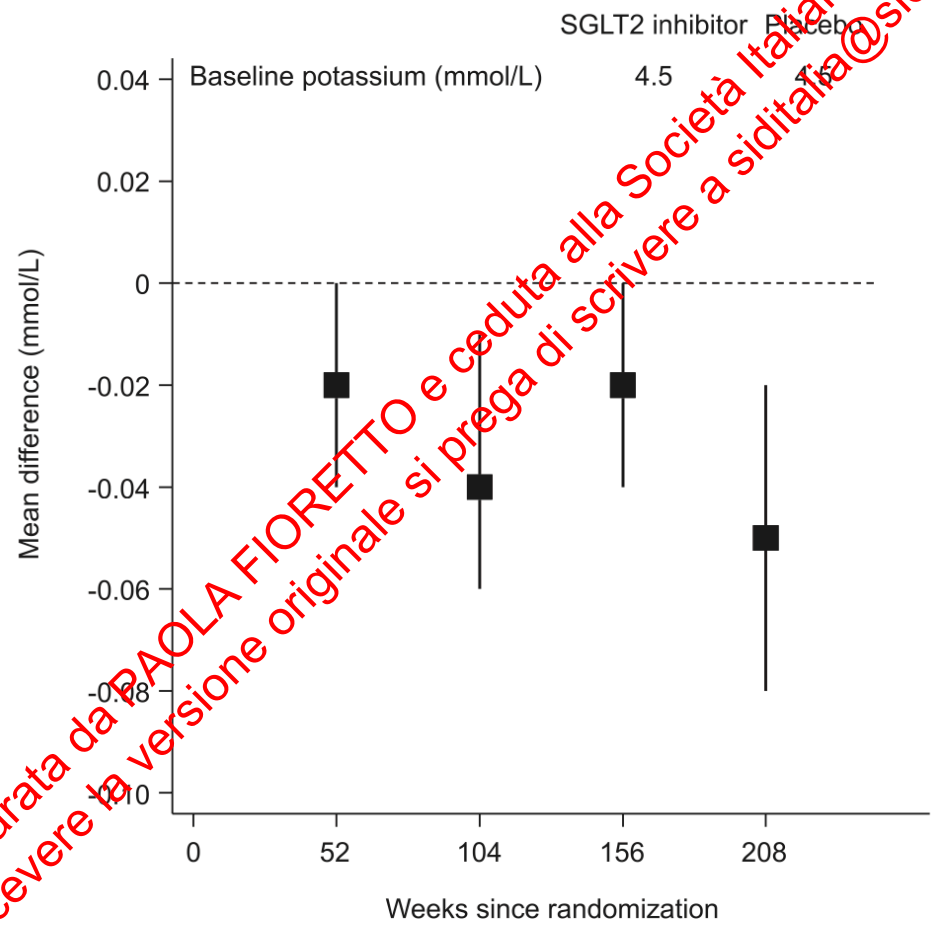
Overall safety outcomes were consistent irrespective of baseline SGLT-2i use

Treatment-emergent AE, n (%)	No SGLT-2i		SGLT-2i	
	Finerenone (n=6072)	Placebo (n=6050)	Finerenone (n=438)	Placebo (n=439)
Any AE	**5204 (85.7)**	**5223 (86.3)**	**398 (90.9)**	**384 (87.5)**
Leading to discontinuation	396 (6.5)	328 (5.4)	18 (4.1)	23 (5.2)
Any SAE	**1914 (31.5)**	**2045 (33.8)**	**146 (33.3)**	**141 (32.1)**
Leading to discontinuation	138 (2.3)	146 (2.4)	7 (1.6)	8 (1.8)
AE resulting in death	**108 (1.8)**	**142 (2.3)**	**2 (0.5)**	**9 (2.1)**
Hyperkalaemia, n (%)				
Any AE	**867 (14.3)**	**436 (7.2)**	**45 (10.3)**	**12 (2.7)**
Leading to discontinuation	105 (1.7)	35 (0.6)	5 (1.1)	3 (0.7)
Leading to hospitalisation	39 (1.4)	8 (0.3)	1 (0.8)	0

Incidence of **hyperkalaemia was lower** in those **receiving an SGLT-2i** at baseline; however, incidence of hyperkalaemia leading to **discontinuation or hospitalisation** was **low across groups**

Rossing P, et al. Diabetes Care 2022

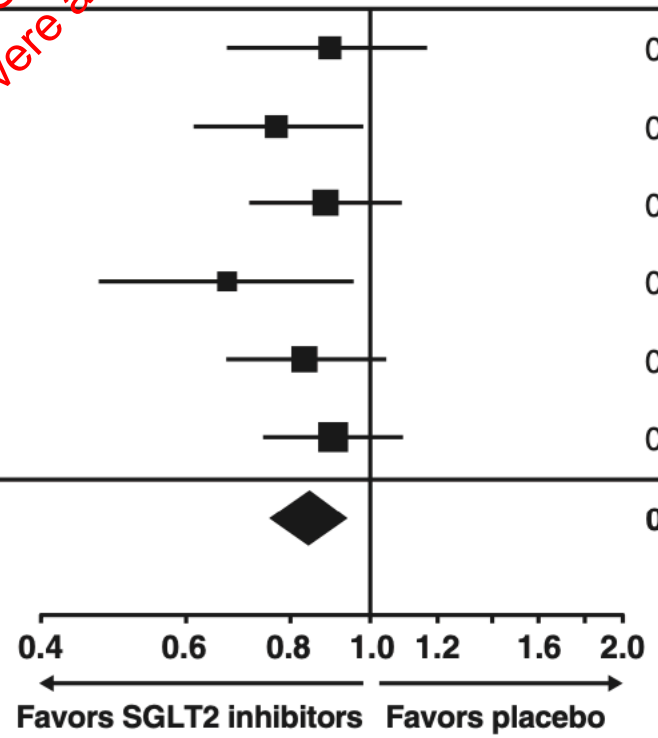
Meta-analysis on SGLT2i and risk of hyperkalemia change from baseline in serum potassium



Neuen BL et al, Circulation, 2022

Meta-analysis on SGLT2i and risk of hyperkalemia effects of SGLT2i on serious htperkalemia

	SGLT2 inhibitors		Placebo		
	n/N	Events per 1000 patient-years	n/N	Events per 1000 patient-years	Hazard Ratio (95% CI)
CANVAS Program	137/5795	8.2	85/4347	9.2	0.89 (0.67, 1.17)
CREDENCE	121/2202	21.6	154/2199	27.9	0.77 (0.61, 0.98)
DAPA-CKD	159/1455	56.9	179/1451	65.3	0.88 (0.71, 1.09)
DECLARE-TIMI 58	53/8582	1.6	78/8578	2.3	0.67 (0.47, 0.95)
EMPA-REG OUTCOME	216/4687	17.2	124/2333	20.5	0.83 (0.67, 1.04)
VERTIS CV	291/5493	18.7	157/2745	21.2	0.90 (0.74, 1.09)
Overall (I^2=0.0%; $P_{heterogeneity}$=0.71)					**0.84 (0.76, 0.93)** P<0.001



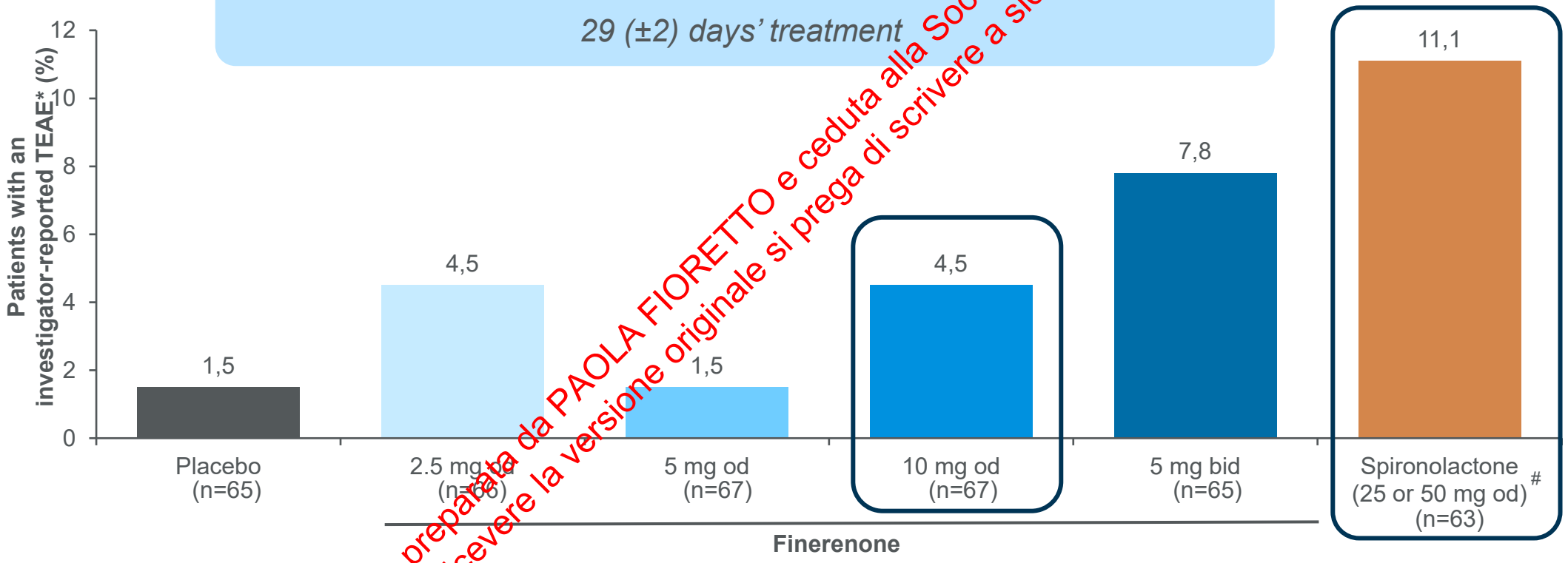
Neuen BL et al, Circulation, 2022

In the phase II ARTS trial, finerenone was associated with lower rates of hyperkalaemia than spironolactone

ARTS Part B (phase II)

Patients with CKD (eGFR 30–60 ml/min/1.73 m²) and HFrEF

29 (±2) days' treatment

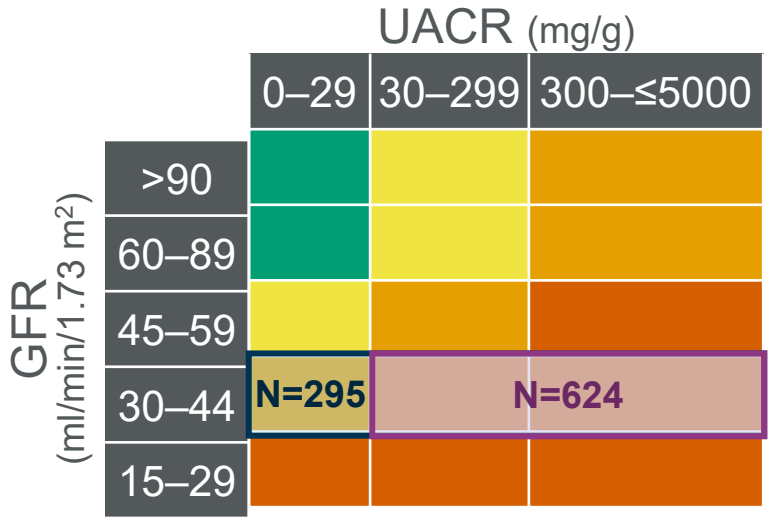


Pitt B, *et al*. *Eur Heart J* 2013;34:2453–2463

Post hoc analysis provided an indirect comparison of the effects of finerenone and spironolactone on SBP and [K⁺] outcomes*,1

To indirectly compare the effects of finerenone and spironolactone on SBP and [K⁺] outcomes in a matched patient population with resistant hypertension and moderate-to-advanced CKD

- **CKD eligibility criteria#**



- **FIDELITY–TRH subgroup** (eGFR and UACR criteria)
- **AMBER** (eGFR criterion only)[2]

- **Other key eligibility criteria**

TRH

- ✓ SBP 135–160 mmHg at baseline
- ✓ ≥3 antihypertensives, including a diuretic and a RASi at baseline
- ✓ Serum [K⁺] 4.3–5.1 mmol/l at baseline

Treated with an NSAID or [K⁺]-affecting medication at baseline

Outcome assessment

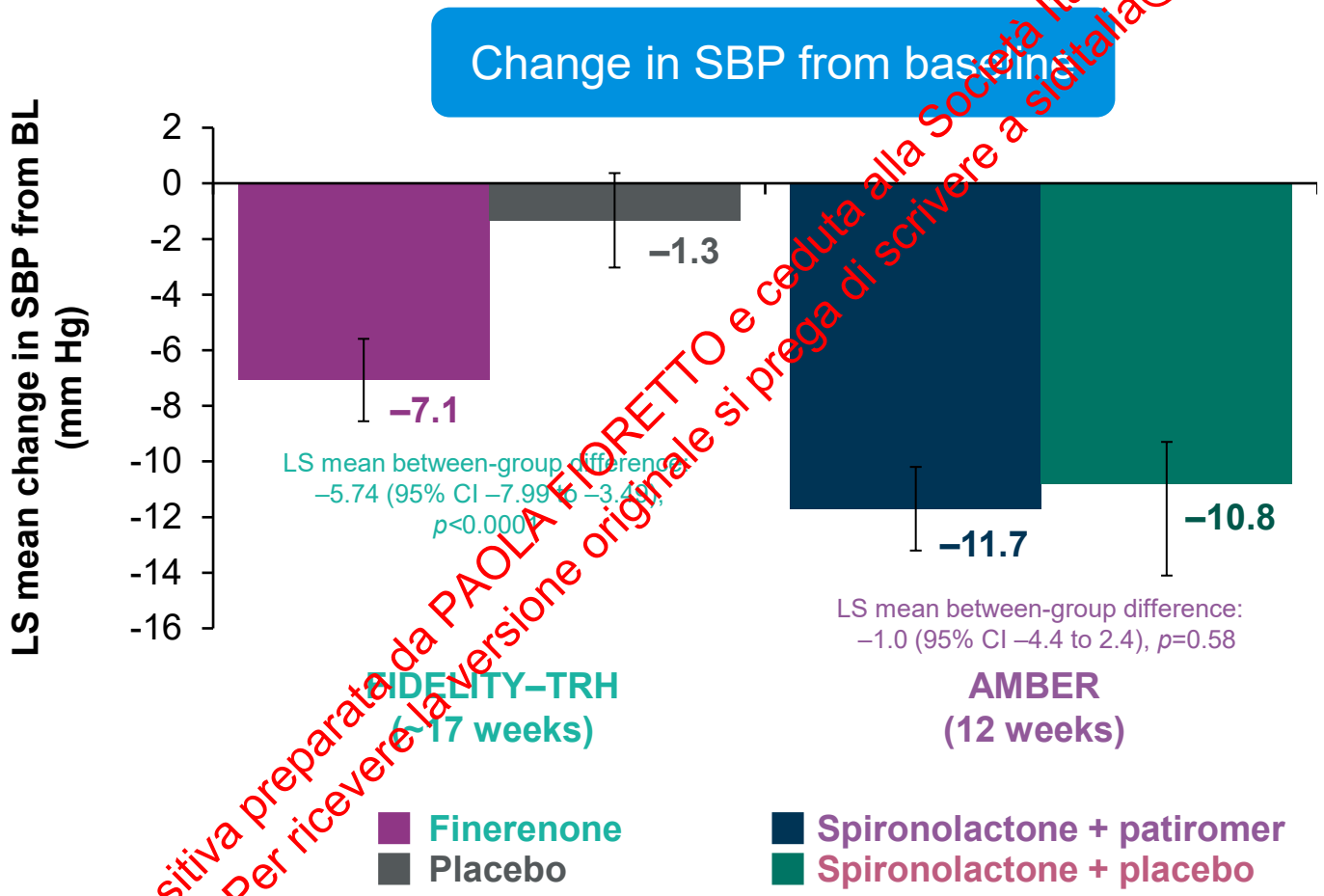
- Change from baseline to month 4 in **SBP**
- Serum [K⁺] ≥5.5 mmol/l
- Hyperkalaemia leading to treatment discontinuation

FIDELITY-TRH
At 4 months (~17 weeks)

AMBER[2]
At 12 weeks

Agarwal R, *et al, Clinical Kidney j, 2022*

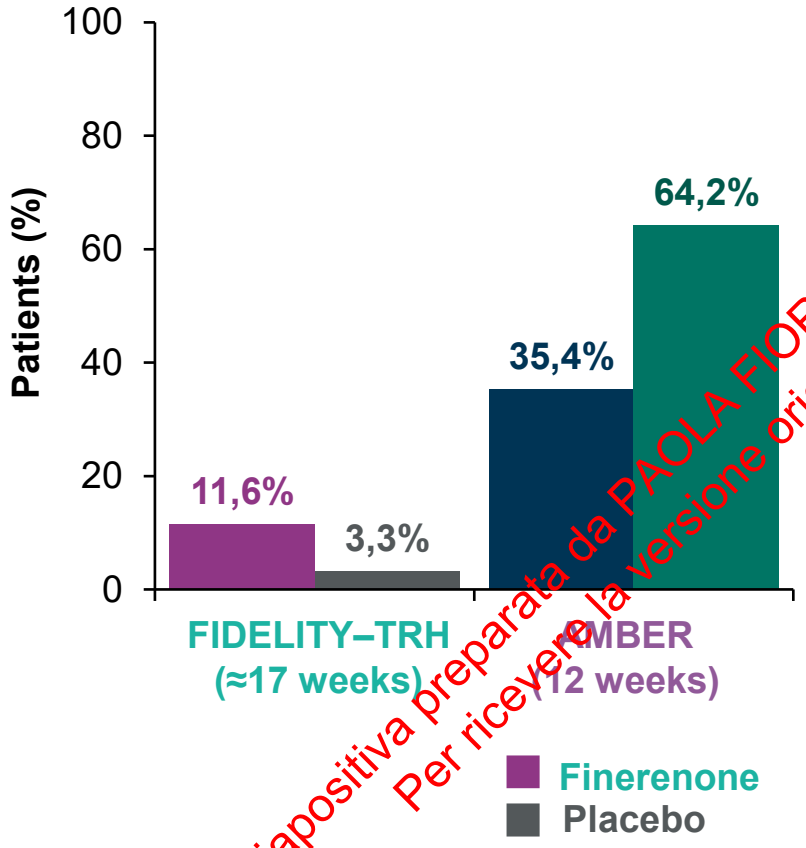
Finerenone is associated with a reduction in SBP, although reductions were smaller than those achieved with spironolactone with or without a potassium binding agent



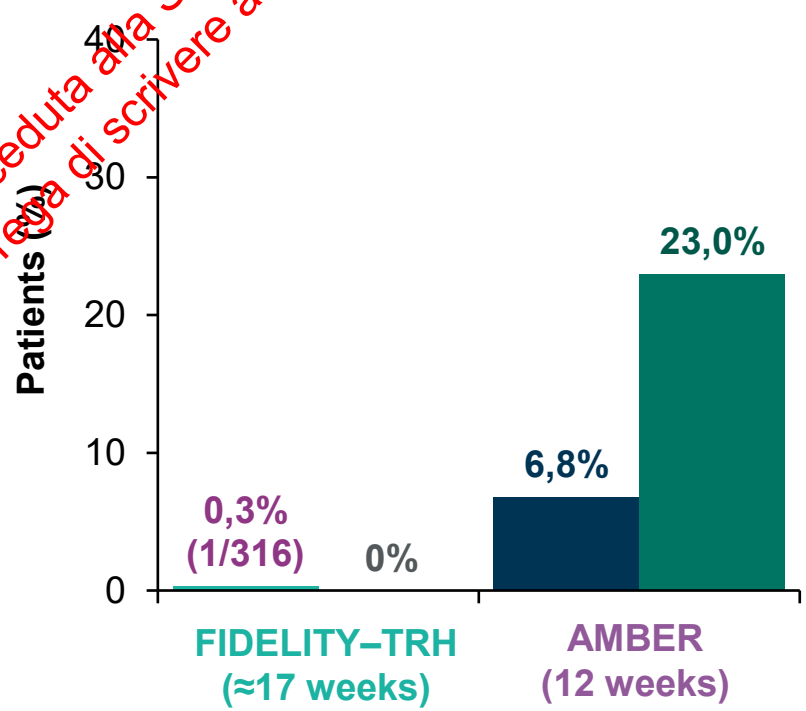
Agarwal R, *et al, Clinical Kidney j, 2022*

Finerenone may be associated with a lower risk of hyperkalaemia than spironolactone ± potassium-binding agent during the first 4 months of treatment

Incidence of serum [K^+] ≥5.5 mmol/l



Treatment discontinuation due to hyperkalaemia



Agarwal R, *et al, Clinical Kidney j, 2022*

JAMA Network | Open

Original Investigation | Pulmonary Medicine

Association of Finerenone Use With Reduction in Treatment-Emergent Pneumonia and COVID-19 Adverse Events Among Patients With Type 2 Diabetes and Chronic Kidney Disease

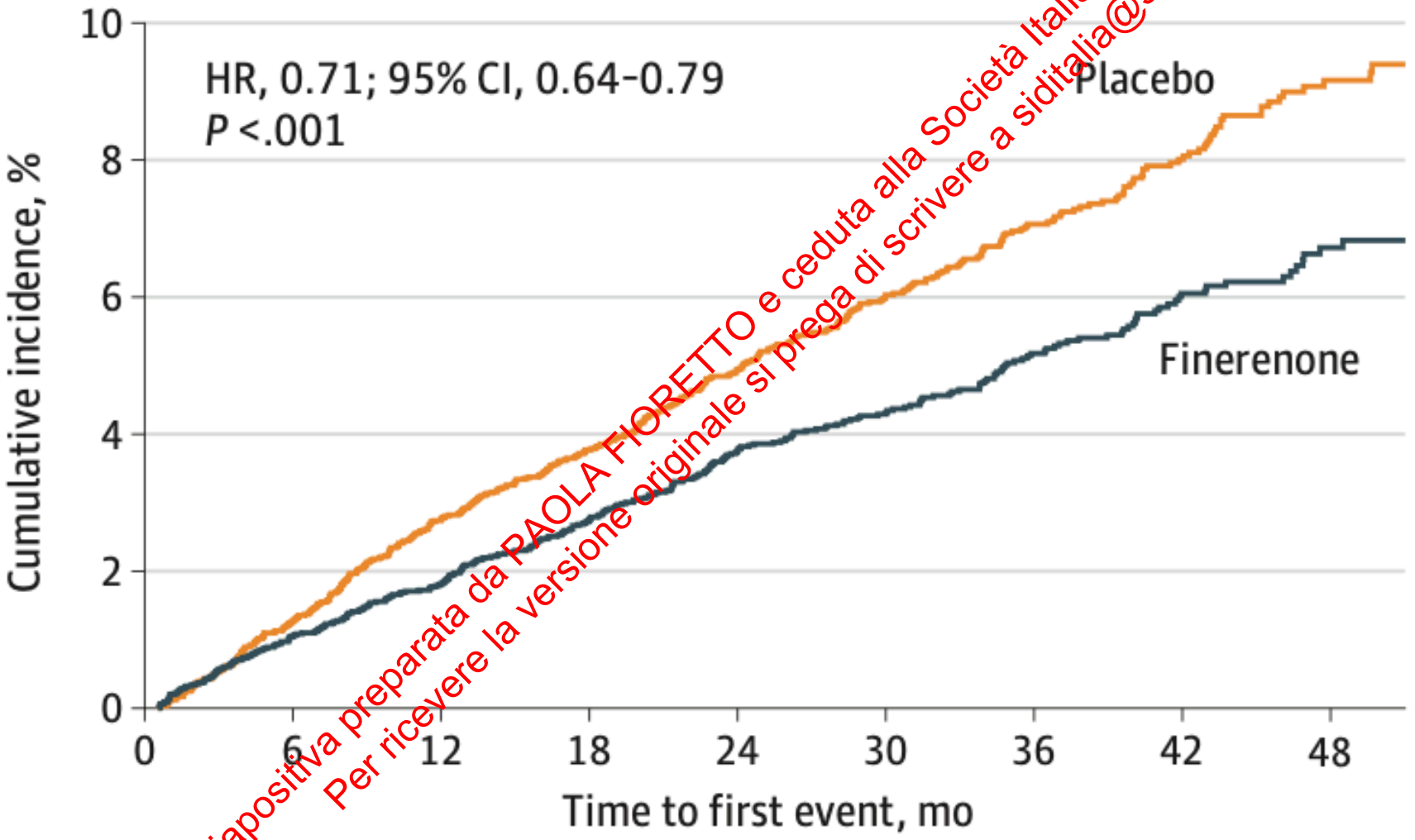
A FIDELITY Pooled Secondary Analysis

Bertram Pitt, MD; Rajiv Agarwal, MD; Stefan D. Anker, MD; Luis M. Ruilope, MD; Peter Rossing, MD; Christiane Ahlers, DiplStat; Meike Brinker, MD; Amer Joseph, MBBS; Marc Lambelet, DiplMath; Robert Lawatscheck, MD; Gerasimos S. Filippatos, MD; for the FIDELIO-DKD and FIGARO-DKD Investigators

Table 2. Treatment-Emergent Pneumonia and COVID-19 AEs in the FIDELITY and FIGARO-DKD Safety-Evaluable Populations

Outcome	Finerenone		Placebo		HR (95% CI)	*P* value[a]
	Patients, No. (%)	Events, No./100 PY	Patients, No. (%)	Events, No./100 PY		
FIDELITY						
No.	6510	NA	6489	NA	NA	NA
Pneumonia[b]						
AE	307 (4.7)	1.88	434 (6.7)	2.64	0.71 (0.64-0.79)	<.001
SAE	171 (2.6)	1.03	250 (3.9)	1.50	0.69 (0.60-0.79)	<.001
Fatal AE	10 (0.2)	0.06	13 (0.2)	0.08	0.78 (0.44-1.40)	.41
COVID-19[b]						
AE	86 (1.3)	0.43	118 (1.8)	0.59	0.73 (0.60-0.89)	.002
SAE	38 (0.6)	0.19	61 (0.9)	0.30	0.63 (0.47-0.83)	.001
Fatal AE	14 (0.2)	0.07	19 (0.3)	0.09	0.74 (0.46-1.21)	.23

TIME TO TREATMENT EMERGENT PNEUMONIA



Ongoing studies with Finerenone

Trial Name	NCT Number	Indication	Planned Enrollment	Primary Endpoint	Estimated Study Completion
FINE-REAL	NCT05348733	CKD and T2D	4000	Treatment patterns *	February 2026
CONFIDENCE	NCT05254002	CKD and T2D	807	Relative change in UACR from baseline to 180 days	January 2024
FIND-CKD	NCT05047263	Nondiabetic CKD	1580	Mean rate change of total eGFR slope from baseline to month 32	December 2025
FIONA	NCT05196035	Pediatric CKD	219	≥30% UPCR reduction from baseline to day 180	September 2026
FINEARTS-HF	NCT04435626	HF with LVEF ≥40%	5500	CV death and HF events	May 2024

Kolkhof P et al, Int J of Molecular Sciences, 2022

Recommendations of Finerenone use in diabetic chronic kidney disease

Scientific Society	Year	Recommendation	Grade
American Diabetes Association	2023	In people with chronic kidney disease and albuminuria who are at increased risk for cardiovascular events or chronic kidney disease progression, a nonsteroidal mineralocorticoid receptor antagonist shown to be effective in clinical trials is recommended to reduce chronic kidney disease progression and cardiovascular events. [recommendation 11.5d]	A
American Diabetes Association & KDIGO consensus	2022	A nonsteroidal mineralocorticoid receptor antagonist (ns-MRA) with proven kidney and cardiovascular benefit is recommended for patients with T2D, eGFR ≥25 mL/min/1.73m2, normal serum potassium concentration, and albuminuria (albumin-to-creatinine ratio [ACR] ≥30 mg/g) despite maximum tolerated dose of renin-angiotensin system (RAS) inhibitor	-
KDIGO	2022	We suggest a nonsteroidal mineralocorticoid receptor antagonist with proven kidney or cardiovascular benefit for patients with T2D, an eGFR ≥25 ml/min per 1.73 m2, normal serum potassium concentration, and albuminuria (≥30 mg/g [≥3 mg/mmol]) despite maximum tolerated dose of RAS inhibitor [recommendation 1.4.1]	2A
AACE American Association of Clinical Endocrinology	2022	A non-steroidal mineralocorticoid receptor antagonist (finerenone) with proven kidney and CVD benefit is recommended for persons with T2D, an eGFR ≥25 mL/min/1.73 m2, normal serum potassium concentration, and albuminuria (ACR ≥30 mg/g) despite a maximum tolerated dose of a renin-angiotensin system inhibitor [recommendation 6.6]	1A

1. American Diabetes Association Professional Practice Committee, Diabetes Care 2022;45(1); https://doi.org/10.2337/dc22-S011; 2. De Boer HI et al., Diabetes Care 2022; DOI: 10.2337/dci22-0027; 3. KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease, Kidney Int 2022; 102(55); 4. Blonde L et al., Endocrine Practice 2022, in press; https://doi.org/10.1016/j.eprac.2022.08.002